

**CLAIMS:**

1. An integrated lab-on-a-chip diagnostic system for carrying out a sample preparation process on a fluid sample containing cells and/or particles, the system comprising:
- 5 (a) an inlet for a fluid sample;
- (b) a lysis unit for lysis of cells and/or particles contained in the fluid sample;
- (c) a nucleic acid extraction unit for extraction of nucleic acids from the cells and/or particles contained in the fluid sample;
- 10 (d) a reservoir containing a lysis fluid;
- (e) a reservoir containing an eluent for removing nucleic acids collected in the nucleic acid extraction unit;
- 15 wherein the sample inlet is in fluid communication with the lysis unit, an optional valve being present to control the flow of fluid therebetween;
- wherein the lysis unit is in fluid communication with the nucleic acid extraction unit, an optional valve being present to control the flow of fluid therebetween;
- 20 wherein the reservoir containing the lysis fluid is in fluid communication with the lysis unit, an optional valve being present to control the flow of fluid therebetween; and
- wherein the reservoir containing the eluent is in fluid communication with the nucleic acid extraction unit, an optional valve being present to control the flow of fluid therebetween.
- 25
2. A system as claimed in claim 1, wherein the reservoir containing the lysis fluid is in fluid communication with the inlet, an optional valve being present to control the flow of fluid therebetween.
- 30

3. A system as claimed in claim 1 or claim 2, wherein the reservoir containing the eluent is in fluid communication with the inlet, an optional valve being present to control the flow of fluid therebetween.
4. A system as claimed in any one of claims 1 to 3, further comprising (g) a nucleic acid reaction unit, preferably a nucleic acid sequence amplification and detection unit, wherein the nucleic acid extraction unit is in fluid communication with the nucleic acid reaction unit, an optional valve being present to control the flow of fluid therebetween.
5. A system as claimed in any one of claims 1 to 4, further comprising (h) a waste unit, wherein the waste unit is in fluid communication with the lysis unit, an optional valve being present to control the flow of fluid therebetween.
6. A system as claimed in any one of claims 1 to 5, further comprising (i) a reservoir containing a washing solvent, preferably ethanol, which reservoir is in fluid communication with the nucleic acid extraction unit, an optional valve being present to control the flow of fluid therebetween.
7. A system as claimed in any one of claims 1 to 6, further comprising (j) a reservoir containing a further washing solvent, preferably isopropanol, which reservoir is in fluid communication with the nucleic acid extraction unit, an optional valve being present to control the flow of fluid therebetween.

- 44 -

8. A system as claimed in claim 6 or claim 7, wherein the reservoir containing the eluent is in fluid communication with the reservoir containing the first washing solvent  
5 and/or the reservoir containing the second washing solvent.

9. A system as claimed in claim 8, wherein the eluent, the first washing solvent and/or the second washing solvent are contained in a common reservoir.

10

10. A system as claimed in claim 9, wherein the eluent, the first washing solvent and/or the second washing solvent are separated from one another in the common reservoir by a fluid, preferably air.

15

11. A system as claimed in claim 9 or claim 10, wherein the common reservoir comprises a conduit in fluid communication with the inlet and the lysis unit.

20 12. A system as claimed in any one of claims 1 to 11, further comprising (k) means for introducing a fluid sample and/or air into the inlet, said mean preferably comprising a pump or a syringe.

25 13. A system as claimed in any one of claims 1 to 11, further comprising a filtration unit, which unit is in fluid communication with the lysis unit.

30 14. A system as claimed in claim 13, wherein the filtration unit comprises one or more of a dead-end filter, a cross-flow filter (eg micro-structured channels, porous hollow fibres or membranes), a gravity settler, a centrifuge, an

- 45 -

acoustic cell filter, an optical trap, dielectrophoresis (DEP), electrophoresis, flow cytometry and adsorption based methods.

5 15. A system as claimed in any one of claims 1 to 11, wherein the lysis unit further comprises means to filter the fluid sample.

10 16. A system as claimed in claim 15, wherein said means comprises one or more of a dead-end filter, a cross-flow filter (eg micro-structured channels, porous hollow fibres or membranes), a gravity settler, a centrifuge, an acoustic cell filter, an optical trap, dielectrophoresis (DEP), electrophoresis, flow cytometry and adsorption based  
15 methods.

17. A system as claimed in any one of the preceding claims, wherein the system further comprises means for heating the contents of the lysis unit and/or the nucleic acid  
20 extraction unit.

18. A system as claimed in claim 17, wherein said mean comprises one or more Peltier elements located in or adjacent the lysis unit and/or the nucleic acid extraction  
25 unit.

19. A system as claimed in any one of the preceding claims, wherein the nucleic acid extraction unit is at least partially filled with silica beads or particles.

30

20. A system as claimed in claim 19, wherein the nucleic acid extraction unit further comprises one or more sets of

- 46 -

electrodes adjacent the silica beads or particles for collecting and/or preconcentrating the eluted nucleic acids.

21. A system as claimed in claim 20, wherein said one or  
5 more sets of electrodes comprises platinum electrodes.

22. A system as claimed in any one of the preceding claims for extracting nucleic acids present in a biological fluid, a dairy product, an environmental fluid or drinking water.

10

23. An apparatus for the analysis of biological and/or environmental samples, the apparatus comprising a system as defined in any one of the preceding claims.

15 24. An assay kit for the analysis of biological and/or environmental samples, the kit comprising a system as defined in an one of the claims 1 to 22 and means for contacting the sample with the system.

20 25. An apparatus as claimed in claim 23 or an assay kit as claimed in claim 24 which is disposable.

26. A method for the manufacture of an integrated lab-on-a-chip diagnostic system as defined in any one of the  
25 preceding claims, which method comprises:

A. providing a substrate having an inlet recess, a lysis unit recess, a nucleic acid extraction unit recess, a lysis fluid reservoir recess and an eluent reservoir recess in a surface thereof;

30 B. providing a cover; and

C. bonding the cover to the substrate to create the (a) inlet, (b) the lysis unit, (c) the nucleic acid extraction

- 47 -

unit, (d) the lysis fluid reservoir and (e) the eluent reservoir, each being defined by the respective recess in said surface of the substrate and the adjacent surface of the cover.

5

27. A method as claimed in claim 26, further comprising the step of introducing lysis fluid into the lysis fluid reservoir either before or after bonding the cover to the substrate.

10

28. A method as claimed in claim 26 or claim 27, further comprising the step of introducing eluent into the eluent reservoir either before or after bonding the cover to the substrate.

15

29. A method as claimed in any one of claims 26 to 28, further comprising the step of introducing a first washing solvent, preferably ethanol, into the eluent reservoir either before or after bonding the cover to the substrate.

20

30. A method as claimed in any one of claims 26 to 29, further comprising the step of introducing a second washing solvent, preferably isopropanol, into the eluent reservoir either before or after bonding the cover to the substrate.

25

31. A method as claimed in any one of claims 26 to 30, wherein the eluent, and/or the first washing solvent and/or the second washing solvent are separated from one another by a fluid, preferably air.

30

32. A method as claimed in claim 26 or claim 27, further comprising:

- 48 -

introducing eluent into the eluent reservoir after  
bonding the cover to the substrate;

introducing a first volume of an immiscible fluid,  
preferably air, into the eluent reservoir;

5     introducing a first washing solvent, preferably ethanol,  
into the eluent reservoir, whereby the first washing solvent  
is separated from the eluent by said first volume of  
immiscible fluid;

introducing a second volume of immiscible fluid,  
10   preferably air, into the eluent reservoir; and

introducing a second washing solvent, preferably  
isopropanol, into the eluent reservoir, whereby the second  
washing solvent is separated from the first washing solvent  
by said second volume of immiscible fluid.

15

20

25

30